
CLOZAPINE TREATMENT IN PATIENTS LIVING IN THE COMMUNITY

Karl Schembri, Lilian M. Azzopardi

Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida

Corresponding author: Karl Schembri

Email: karlschembri87@hotmail.com

ABSTRACT

OBJECTIVE The aim of this study was to assess clozapine treatment in the local community with respect to patient monitoring during dispensing, patient compliance through prescription refills, presence of any other existing co-morbidities and presence of potential drug-drug interactions.

METHOD An audit on whether pharmacy personnel check patients' white blood cell count and absolute neutrophil count prior to dispensing was performed. A total of 100 audits were carried out. A computer programme entitled 'Pharmacy Dispensing System' was used to assess patient compliance through prescription refills over a 3-month period. Another computer programme entitled 'Schedule V' was used to determine any other co-morbidities. After determining the list of all the chronic medications, analysis of the presence of any potential drug-drug interactions was undertaken. The 'Drug Interaction Checker', a drug interaction database provided by RxList, was used. This database classified potential drug-drug interactions into 3 categories namely minor, significant and serious.

KEY FINDINGS The white blood cell count and absolute neutrophil count were checked in all instances (N=100), however this intervention was not documented. Over a 3-month period, 78 out of 90 patients were compliant. Diabetes was the most common co-morbidity (n=15) and 76 patients receiving clozapine may be exposed to a potential drug-drug interaction. A total of 363 possible drug interactions were present in this group of patients. The most common type of potential drug-drug interaction fell in the 'significant drug-drug interactions' category (n=289).

CONCLUSION Patient monitoring was carried out, however documentation processes need to be elaborated. Identification of drug interactions is of utmost importance since certain interactions can be dangerous. Apart from detecting drug interactions, discussion with other healthcare professionals should be undertaken to assess the possibility of replacing such interacting drugs with alternative options. This measure should be carried out to promote patient safety.

KEYWORDS clozapine, patient monitoring, co-morbidities, drug-drug interactions

INTRODUCTION

Clozapine is an atypical antipsychotic used in treatment-resistant schizophrenia.¹ In Malta patients who are on this drug and live in the community collect this medication from the Outpatients Pharmacy at Mater Dei Hospital. The maximum supply of clozapine dispensed is for 28 days. Since clozapine causes agranulocytosis², the white blood cell count and absolute neutrophil count have to be checked prior to dispensing. The occurrence of potential drug-drug interactions is quite common in psychiatric patients since a large number of antipsychotics are metabolised through the hepatic cytochrome P450 system.³

The aim of this study was to review clozapine treatment in patients living in the community with respect to undertaking of patient monitoring during dispensing, assessment of patient compliance to clozapine treatment through prescription refills, determination of the presence of any other co-morbidities and assessment of the presence of potential drug-drug interactions.

METHOD

Approval to carry the study was obtained from the Chief Executive Officer and the Head of the Pharmacy Department at Mater Dei Hospital, as well as the Data Protection Officers of both Mater Dei Hospital and the Directorate of Pharmaceutical Affairs.

A form entitled 'Audit Form for Patient Monitoring' was designed to evaluate patient monitoring. Observation of whether the pharmacist or pharmacy technician dispensing clozapine checked the white blood cell and absolute neutrophil count was undertaken. Another procedure observed was whether the pharmacist in charge of the high security store carries out double checking with regards to the mentioned parameters in the complete blood count. The audit was repeated 100 times.

Since compliance to clozapine was assessed through prescription refills, the computer programme entitled 'Pharmacy Dispensing System' was used. This programme is useful since it keeps records of any medication collected from Mater Dei Hospital. Clozapine compliance was retrospectively assessed over a 3-month period.



The Schedule V program is a computer programme which can be used to determine the list of chronic conditions the patient is suffering from. The number of co-morbidities present in each patient and the number of patients suffering from a particular co-morbidity was obtained. The medicines entitlement was used to obtain any other chronic medication/s the patient was taking during the selected 3-month period. After determining the list of medications, analysis for the occurrence of any potential drug-drug interactions was carried out. The drug interaction database used in this study was the 'Drug Interaction Checker' provided by RxList.⁴ The frequency of patients experiencing a potential drug-drug interaction and the mean number of potential drug-drug interactions occurring in each patient were determined. The drug interaction database classified such potential drug-drug interactions into 3 categories, namely minor, significant and serious. The total number of potential drug-drug interactions and the total number of potential drug-drug interaction combinations in each category were determined.

RESULTS

The white blood cell count and absolute neutrophil count were checked in all instances (N=100) by the pharmacist or pharmacy technician dispensing the medication, as well as by the pharmacist in charge of the high security store.

A total of 90 patients were included in the study, where 47 were female and 43 were male. The mean age of the patients was 50 years (range 20-80 years). Patient compliance to clozapine was assessed through prescription refills, where 78 out of 90 patients were compliant. The majority of patients (n=54) did not suffer from any other co-morbidities (Figure 1).

The most common (n=15) co-morbidity present was diabetes (Figure 2). The co-morbidities classified as 'Others' included gastro-oesophageal reflux disease (n=1), hypoparathyroidism (n=1), genetic dyslipidaemia (n=2), peripheral vascular disease (n=1), gastric ulcers (n=2), arrhythmias (n=1), myasthenia gravis (n=1) and cerebrovascular disease (n=1).

The most common drug taken by the patients in combination with clozapine was paroxetine (n=17) (Figure 3).

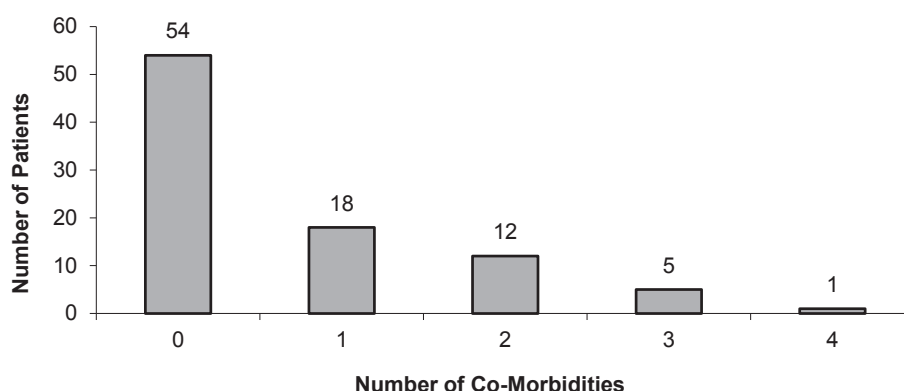


Figure 1: Number of co-morbidities present in clozapine-treated patients (N=90)

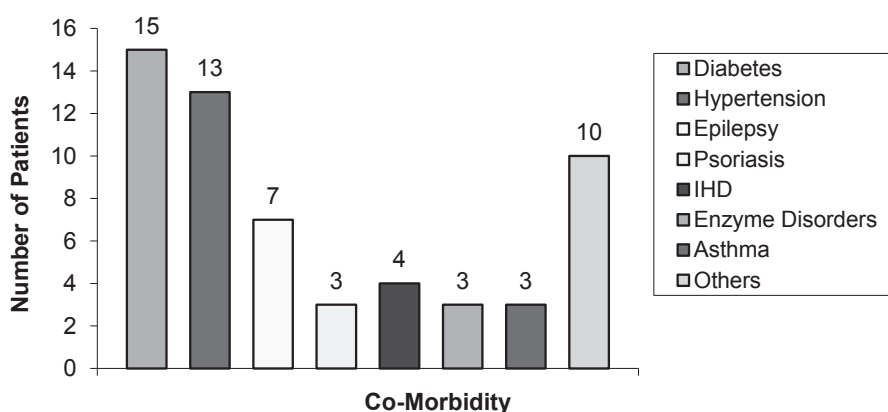


Figure 2: Frequency of the different co-morbidities in clozapine patients living in the community (N=90)

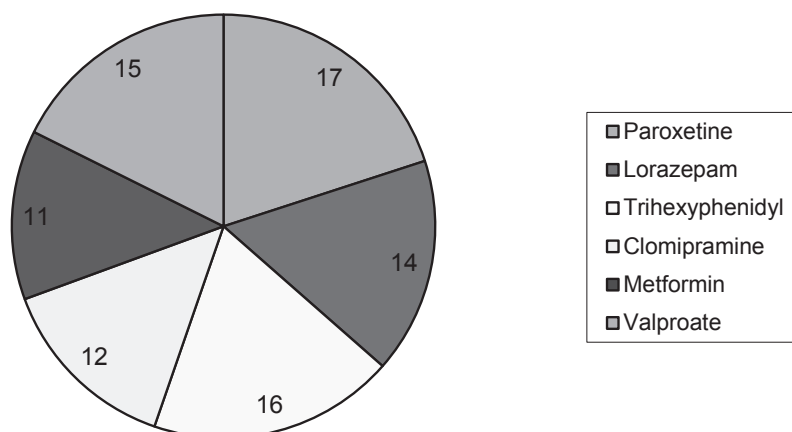


Figure 3: Frequency of the 6 most common drugs taken together with clozapine (N=90)

A total of 363 potential drug-drug interactions were identified in these patients. Out of 90 patients, 76 patients could be exposed to drug interactions. The mean number of potential drug-drug interactions present in each patient is 4. 'Significant' drug-drug interactions (n=289) are the most common type of potential drug-drug interactions. This is followed by 'minor' drug-drug interactions (n=54) and 'serious' drug-drug interactions (n=20).

DISCUSSION

Even though the white blood cell and absolute neutrophil count were checked in all instances, this intervention was not documented. Documentation of an intervention is important since it provides a way for the pharmacist to be responsible for his or her actions. It also provides a means of communication with other healthcare professionals during the planning of patient care. Documentation must be complete, factual, current, and organised.⁵ The computer programme 'Pharmacy Dispensing System' can be used to document this intervention to ensure that good documentation is maintained. The person dispensing the medication can document this process under the remarks section by writing the values for the white blood cell and absolute neutrophil count and whether the values are within the required limits. When the transaction is complete, a sticker with this information, together with the amount of medications dispensed, is produced and fixed on the back of the patient's Schedule V Card. The professional dispensing the medication can sign on this sticker, followed by a counter signature by the pharmacist who double checks this intervention. This procedure would ensure that the patient and health care professionals who view the patient's Schedule V card would be aware that the patient's white blood cell and absolute neutrophil count are being monitored.

There are various reasons which explain the reason for diabetes being a common occurrence in schizophrenic patients. Clozapine has various side-effects including hyperglycemia, weight gain, hypercholesterolemia and hypertriglyceridemia.⁶ These side-effects increase the patient's risk of developing diabetes. Another reason why diabetes is the most common co-morbidity is that there is a relationship between schizophrenia and diabetes. It has been found that schizophrenic patients are 2 to 4 times more likely to develop diabetes.⁷ Another factor which contributes towards a high incidence of diabetes mellitus is the high occurrence of diabetes in the Maltese population.⁸ The pharmacist should therefore monitor the patient for diabetes mellitus during dispensing.

The occurrence of potential drug-drug interactions may lead to the need for hospitalisation. A study by Raschetti *et al* has shown that the frequency of visits to the emergency department due to drug-drug interactions represented 3.8% of the total visits.⁹ Having a clinical pharmacist assigned to psychiatric consultants is recommended to reduce the potential occurrence of drug-related problems and to provide information about interactions to physicians and patients. At present, there are no clinical pharmacists forming part of the psychiatric team at Mater Dei Hospital. Pharmacists are in an ideal position to give advice about the occurrence of potential drug-drug interactions.

A limitation of this study was the method chosen to determine patient compliance. The determination of the rate of prescription refills is not expensive and easy to carry out, however, this method is not as accurate as direct observation of patient compliance to treatment. Another limitation was that only chronic drugs which are collected for free were considered for the occurrence of potential drug-drug interactions. Drugs which the patient might purchase were not included.



Having a clinical pharmacist assigned to psychiatric consultants is recommended to reduce the potential occurrence of drug-related problems and to provide information about interactions to physicians and patients.

CONCLUSION

Patient adherence to medication is necessary to achieve the maximal therapeutic benefit. Since certain drug-drug interactions can be dangerous, it is important that interactions are detected. Besides detecting drug-drug interactions, discussion with other healthcare professionals regarding clozapine treatment and therapies used for co-morbidities should be carried out to assess the possibility of replacing the interacting drug with alternative treatment options. The introduction of such a procedure will help to further promote patient safety.

References

1. Kane J, Honigfeld G, Singer J, Meltzer H. Clozapine for the treatment-resistant schizophrenic: A double-blind comparison with chlorpromazine. *Arch Gen Psychiatry*. 1988;45(9):789-96.
2. Young CR, Bowers MB Jr, Mazure CM. Management of adverse effects of clozapine. *Schizophr Bull*. 1998;24(3):381-90.
3. Guo JJ, Jasmanda W, Kelton CML, Jing Y, Fan H, Keck PE, et al. Exposure to potentially dangerous drug-drug interactions involving antipsychotics. *Psychiatr Serv*. 2012;63(11):1080-88.
4. RxList. Drug Interaction Checker [Online]. 2013 [cited 2013 Dec 7]. Available from: www.rxlist.com/drug-interaction-checker.htm
5. Ontario College of Pharmacists. Documentation Guidelines [Online]. 2012 [cited 2013 Nov 12]. Available from URL: www.ocpinfo.com/regulations-standards/policies-guidelines/documentation-guidelines/
6. EMC+. Summary of Product Characteristics [Online]. 2013 [cited 2014 Mar 15]. Available from: www.medicines.org.uk/emc/medicine/1277/SPC/Clozaril+25mg+and+100mg+Tablets
7. Expert Group. 'Schizophrenia and diabetes 2003' Expert Consensus Meeting, Dublin, 3-4 October 2003: consensus summary. *Br J Psychiatry Suppl*. 2004;47:S112-4.
8. Vella F. Malta has highest rates of diabetes in the EU. Malta Independent [Online]. 2009 Nov 15 [cited 2013 Oct 12]. Available from: www.independent.com.mt/articles/2009-11-15/news/malta-has-highest-rate-of-diabetes-in-the-eu-266296/
9. Raschetti R, Morgutti M, Mennitti-Ippolito F, Belisari A, Rossignoli A, Longhini P, et al. Suspected adverse drug events requiring emergency department visits or hospital admissions. *Eur J Clin Pharmacol* 1999;54(12):959-63.